

REMARKS

This Amendment is submitted in reply to the final Office Action mailed on July 28, 2008. A petition for a one month extension of time is submitted herewith. The Director is authorized to charge the amount of \$130.00 for the cost of the petition for a one month extension of time and any additional fees which may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 112701-727 on the account statement.

Claims 1-4 and 6-11 are pending in this application. Claim 5 was previously canceled. In the Office Action, Claims 1-4 and 6-11 are rejected under 35 U.S.C. §112, second paragraph, and under 35 U.S.C. §102. In response Claims 1-3 and 8-10 have been amended. These amendments do not add new matter. In view of the amendments and/or for the reasons set forth below, Applicants respectfully submit that the rejections should be withdrawn.

In the Office Action, Claims 1-4 and 6-11 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Patent Office alleges that the term "large scale up" in Claims 1, 8 and 9 is a relative term which renders the claims and their dependents indefinite. See, Office Action, page 2, lines 9-17. In response, Applicants have amended Claims 1 and 8-9 to recite, in part, a wave induction mechanism comprising a plate that lifts up only between 5 and 50% of the length of the culture chamber and is compatible with large scale up of a culture medium in an amount up to 1000 L. The amendments do not add new matter. The amendments are supported in the specification at, for example, page 4, lines 11-15; page 4, line 27-page 5, line 3; page 5, lines 11-25; page 6, lines 12-26.

As discussed in the specification, the present culture system can be applied for different cultures with a very easy scale-up from small bag to large bags since the wave induction mechanism is very simple. Specifically, the wave induction mechanism consists of a simple up and down mechanical movement of a small plate that is raised periodically with a motor or a ram linked to a timer. When read in view of the specification, the skilled artisan would understand that a large scale up of the present claims involves increasing the amount of culture medium that is contained in the culture chamber. In fact, the specification clearly describes possible shapes

and sizes of the plastic bags that may be used as a culture chamber and states that the culture chamber is capable of holding amounts of up to 1000 L or more of culture medium. Accordingly, Applicants respectfully submit that a large scale up in accordance with the present claims includes amounts of culture medium that are up to 1000 L.

The Patent Office further alleges that Claim 2 is unclear because the elements of Claim 2 can be interpreted several different ways. In response, Applicants have amended Claims 2-3 and 10 to recite, in part, that that the wave induction mechanism of the present claims lifts up a portion of the bottom surface of the culture chamber in order to induce a wave-like motion in the contents of the culture chamber. The amendments do not add new matter. The amendments are supported in the specification at, for example, page 4, line 27-page 5, line 3; page 6, line 31-page 7, line 2.

Applicants respectfully submit that the skilled artisan would understand that the wave induction system actively moves a portion of the surface area (8 to 20%) of the lower part of the culture chamber by lifting it. In other words, the remaining 80 to 92% of the surface area would not be lifted at all when the wave induction system is active. For example, Figures 1 and 2 clearly illustrate a wave induction mechanism 7 and a directional indicator to indicate the direction in which the wave induction mechanism 7 is moved in order to cause the contents of the culture chamber to create a wave for the purposes of aeration. See, specification, Figures 1 and 2. As shown in Figures 1 and 2, the wave induction mechanism 7 only contacts a portion of the surface area of the lower part of the culture chamber (*i.e.*, the wave induction mechanism 7 only contacts a portion of the bottom of the chamber).

With respect to the "portion of the surface area of the lower part of the culture chamber," the specification further describes that the "wave induction mechanism (7) . . . can consist of a plate placed just under at least one extremity of the culture chamber. . . [which] pulls up the extremity of the culture chamber." See, specification, page 4, line 27-page 5, line 3. "[T]he width of the plate is equal to the width of the culture chamber and the length of the plate is between 5 and 50%, more preferably 8 to 20% of the length of the culture chamber." See, specification, page 6, lines 16-19.

Based on the disclosure in the specification including Figures 1 and 2, Applicants respectfully submit that the skilled artisan would immediately appreciate that the claim limitation

“the wave induction system lifts up from 8 to 20% of the surface area of the lower part of the culture chamber” means that the wave induction mechanism (7) contacts from 8 to 20% of the surface area of the bottom of the culture chamber when the wave induction mechanism (7) is either pushed or pulled in a substantially upward direction, as indicated by Figures 1 and 2, in order to lift the culture chamber and create a wave-like movement within the culture chamber.

Based on at least these noted reasons, Applicants believe that Claims 1-4 and 6-11 fully comply with 35 U.S.C. §112, second paragraph. Accordingly, Applicants respectfully request that the rejections of Claims 1-4 and 6-11 under 35 U.S.C. §112 be withdrawn.

In the Office Action, Claims 1-4 and 6-11 are rejected under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 6,190,913 to Singh (“*Singh*”). Claims 1-4 and 6-11 are rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent Publication No. 2005/0063250 to Hubbard (“*Hubbard*”). Applicants respectfully disagree with and traverse these rejections for at least the reasons set forth below.

Applicants have amended independent Claims 1 and 8-9 to recite, in part, a wave induction mechanism comprising a plate that lifts up only between 5 and 50% of the length of the culture chamber and is compatible with large scale up of a culture medium in an amount up to 1000 L. The amendments do not add new matter. The amendments are supported in the specification at, for example, page 4, lines 11-15; page 4, line 27-page 5, line 3; page 5, lines 11-25; page 6, lines 12-26. In an embodiment, the mixing and aeration of the cell culture apparatus can be achieved by inducing intermittent waves from one extremity of cell culture apparatus to the other using a wave induction mechanism. By using the claimed invention, it is possible to manufacture a cell culture apparatus from flexible plastic material and use the apparatus as a disposable system. Moreover, the mixing/aeration mechanism in accordance with the present claims minimizes cell damages usually due to shear stress and small bubbles. Because the wave induction mechanism is simple, the claimed invention allows for easy and efficient scale-up from small scale to a larger one. Such a large-scale, efficient and disposable culture apparatus can largely reduce production costs of biological material such as biomass cells, embryogenic plant cells, metabolites, secondary plant metabolites and/or recombinant molecules. In contrast, Applicants respectfully submit that the cited references fail to disclose or suggest every element of the present claims.

Singh fails to disclose or suggest a wave induction mechanism comprising a plate that lifts up *only* between 5 and 50% of the length of the culture chamber and is compatible with large scale up of a culture medium in an amount up to 1000 L as required, in part, by Claims 1 and 8-9. In contrast, *Singh* is directed to a rocking platform that extends the length of the plastic bag and that moves a bag back and forth thereby inducing a wave-like motion to the liquid contained therein. See, Figures 1-2. This is in direct contrast to the wave induction mechanism of the present invention, which is simple and allows for easy and efficient scale-up from small scale to a larger one. Because *Singh* discloses a rocking platform that extends the length of the plastic bag, *Singh* cannot disclose or suggest a wave induction mechanism comprising a plate that lifts up *only* between 5 and 50% of the length of the culture chamber as required, in part, by independent Claims 1 and 8-9.

Moreover, *Singh* also fails to disclose or suggest a wave induction mechanism that is compatible with large scale up of a culture medium in an amount up to 1000 L as required, in part, by Claims 1 and 8-9. Further, *Singh* fails to even suggest the use of any amount of culture medium in an amount over 500L. Instead, the rocking of *Singh* is obtained using a central axe (See *Singh*, Figures 1-3) and requires a powerful motor to induce the move (especially for large volumes) along with a specific table or apparatus to place the bag. See *Singh*, column 4, lines 7-33. As a result, this limits the size of the bag that can be used in *Singh*. It is unrealistic to imagine a large volume flexible container balancing from one side to the other around the central axe because the entire culture chamber would rock periodically from one side to the other and generate very high pressure on each side, which is incompatible with a large scale up of a culture medium in an amount up to 1000 L as required, in part, by Claims 1 and 8-9.

Similarly, *Hubbard* also fails to disclose or suggest wave induction mechanism comprising a plate that lifts up *only* between 5 and 50% of the length of the culture chamber and is compatible with large scale up of a culture medium in an amount up to 1000 L as required, in part, by Claims 1 and 8-9. *Hubbard* is directed to a pressure bag this is capable of being selectively pressurized and deflated in conjunction with a disposable bio bag such as a fermenter, mixing bag or storage bag. The pressure bag may surround a selected outer portion of the bag or may be contained within an inner portion of such a bag. The pressure bag can be selectively

pressurized and deflated using a pressurizing fluid supply. Accordingly, this type of system does not include a wave induction mechanism that comprises a plate, and is also incompatible with a large scale-up system due to the increasing expenses associated with the increase of gas pressure and power needed to inflate the pressure bags in the larger systems.

In contrast to the cited references, the claimed cell culture apparatus provides an efficient and low cost cell culture apparatus that is compatible with large scale up. For example, the claimed cell culture apparatus does not require lifting up all the volume of the liquid in the bag as in *Singh*, but only a small part of it. Nevertheless, the wave induction mechanism is still able to generate sufficient waves for agitation/aeration of the cell culture. The claimed cell culture apparatus can require only a small motorized arm even in case of large volumes (see specification, page 6, line 27), which is not possible in *Singh*. It is easily possible to build such disposable plastic bioreactors with large volumes in the range of 1000 L by simply lengthening the width and length of the container and regulating the frequency of the wave generation without any change to the basic mechanism, which is not possible in either of the cited references. Finally, the large cell culture containers can be placed on any floor surface without the need for any specific table, container, etc., which is not possible with the cited references.

For at least the reasons discussed above, Applicants respectfully submit that Claims 1 and 8-9 and Claims 2-4, 6-7 and 10-11 that depend from Claims 1 and 8-9 are novel, nonobvious and distinguishable from the cited references.

Accordingly, Applicants respectfully request that the rejections of Claims 1-4 and 6-11 under 35 U.S.C. §102 be withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims which could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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